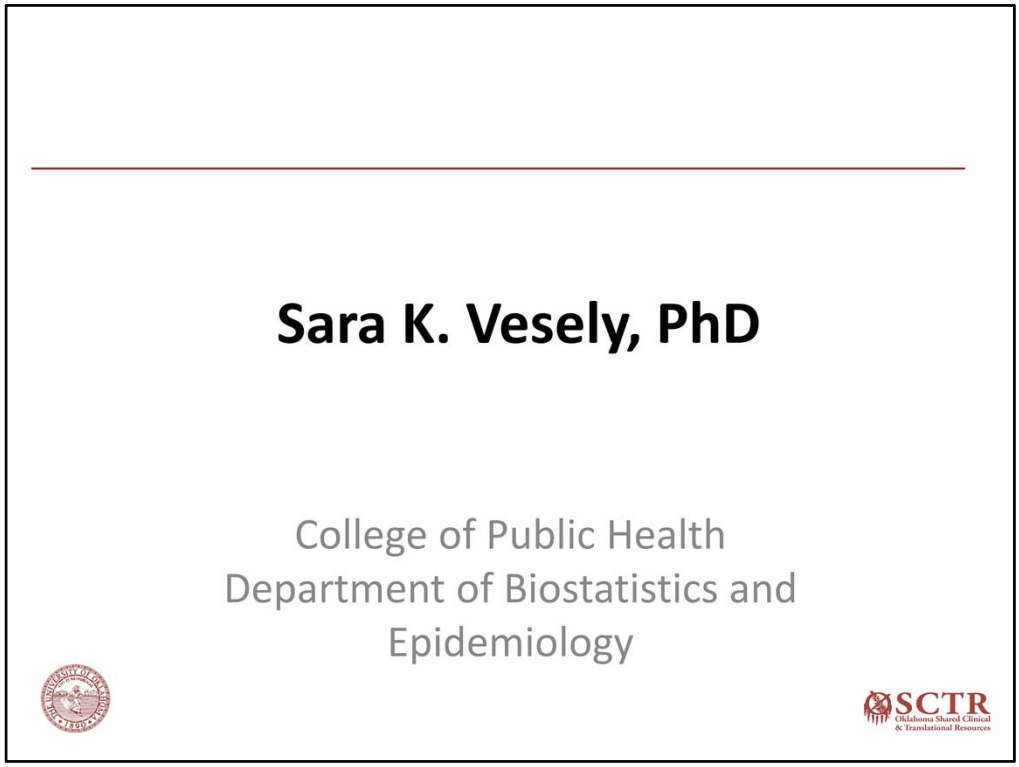

Welcome this video is entitled The Research Question Part I: Terminology. Please do not distribute or copy this video lecture.

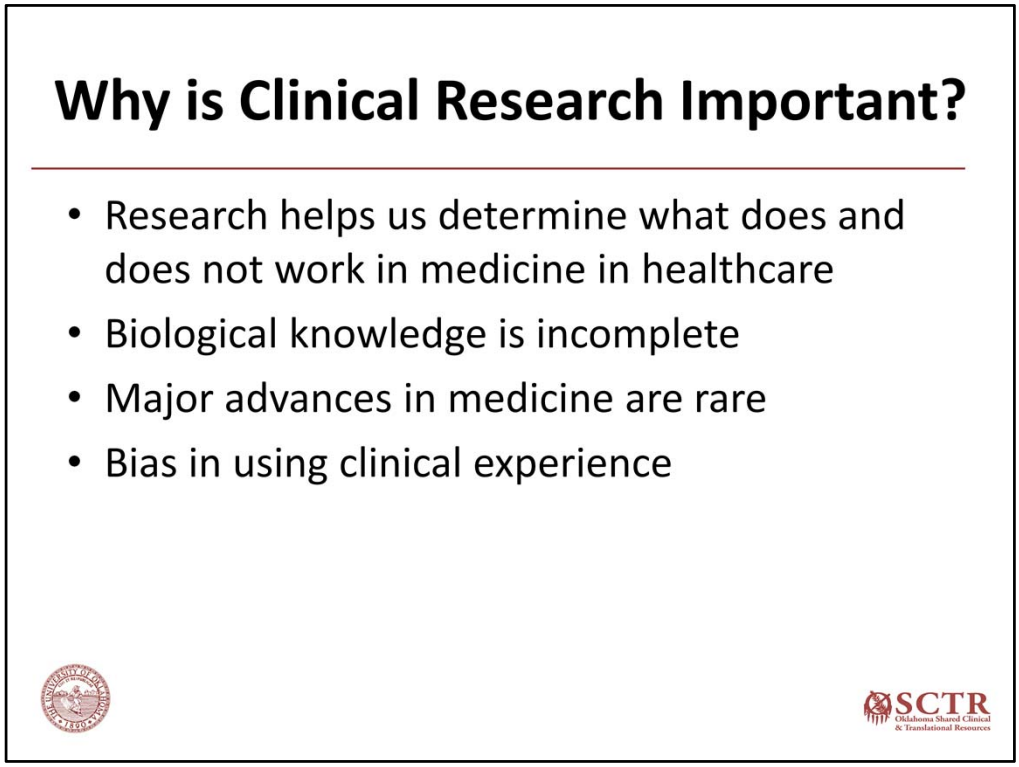



Hello my name is Sara Vesely and I am a professor in the Department of Epidemiology and Biostatistics in the College of Public Health. I am a biostatistician that has been working at the University for over 15 years. I have worked in the areas of benign hematology primarily with Oklahoma TTP-HUS Registry, youth developmental assets, teen pregnancy prevention, and various other projects as a methodological collaborator.

# Outline

- Why is clinical research important?
- Introduction to Terminology
  - Basic Science Research
  - Clinical Research
  - Translational Research
  - Interdisciplinary Research
  - Epidemiology/Biostatistics
  - Study Designs

In this module I will cover the importance of clinical research as well as introduce a wide range of terminology related to the different types of research.




Why is clinical research important? In general research studies helps us determine what does and does not work in medicine and healthcare. It is important to conduct clinical research because at any given time biological knowledge is incomplete. We may know many things about the physiology of disease but we really never know everything. There are new discoveries as well as new tools to measure biological processes that happen frequently. One recent example is the microbiome. Another reason is that major advances in medicine are rare. Antibiotics and insulin in the use of type I diabetics are examples of major advances but other advances in medicine are much smaller and if we don't have a research framework to answer those questions, the determination of whether something new works better is very difficult. Another reason clinical research is imperative is because there's always bias in just using your clinical experience. You may be more likely to either remember the good or bad cases. Also if you are not randomly assigning treatment, the differences you are observing may be related to the patient differences and not treatment differences.

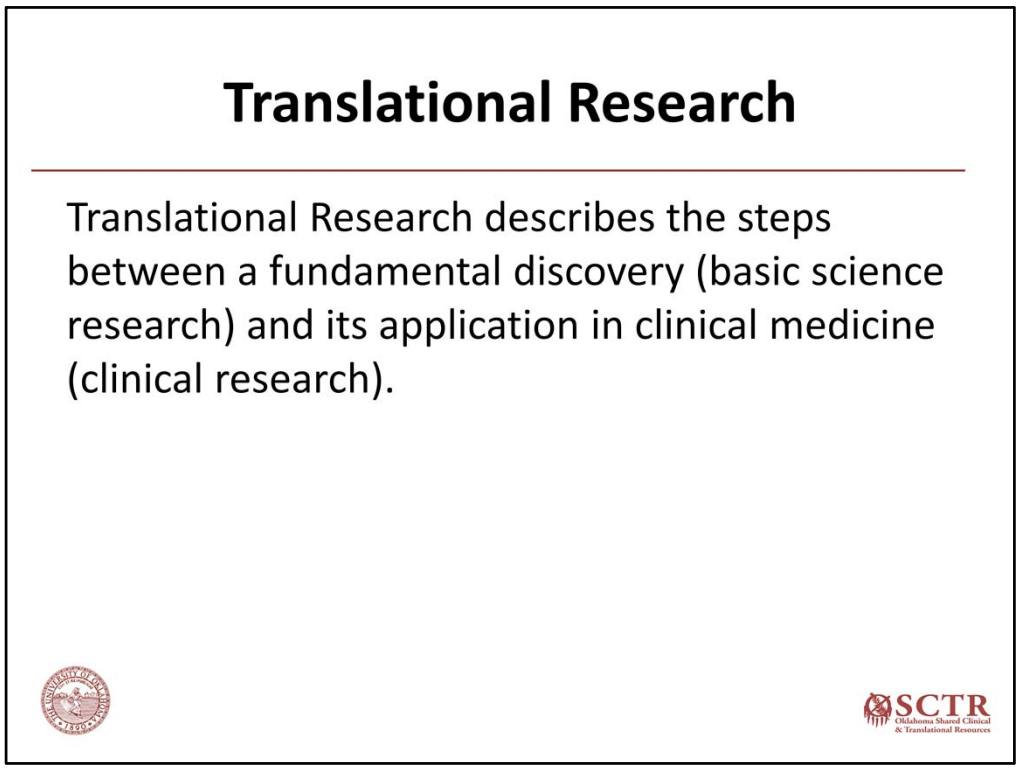
## Basic Science Research

- Basic scientific research is defined as fundamental theoretical or experimental investigative research to advance knowledge without a specifically envisaged or immediately practical application. It is the quest for new knowledge and the exploration of the unknown.

http://www.icsu.org/publications/icsu-position-statements/value-scientific-research

Basic science research is research in which we are looking to know more about fundamental knowledge. Investigators want to make some discovery about some phenomenon in our world. Generally when we think about basic science research the investigators don't have an immediately practical application. Instead they are seeking to learn something about how the world works. This type of research trying to understand exactly how something works it is more of an exploration or quest for new knowledge or to learn more about the unknown.


On the other hand clinical research is very applied. In clinical research we are generally thinking about how something happens in human subjects. Broadly clinical research covers all studies of diseases and trials of treatments that actually take place in human subjects. Another way to think about clinical research is any research that involves human subjects or tissue or material from humans. This may also include not only biological samples but also information about someone's behavior or other patient characteristics.




Translational research is the link between basic science research and clinical research. Translational research figures out how to apply these fundamental discoveries to clinical medicine or clinical research.

# Clinical and Translational Research

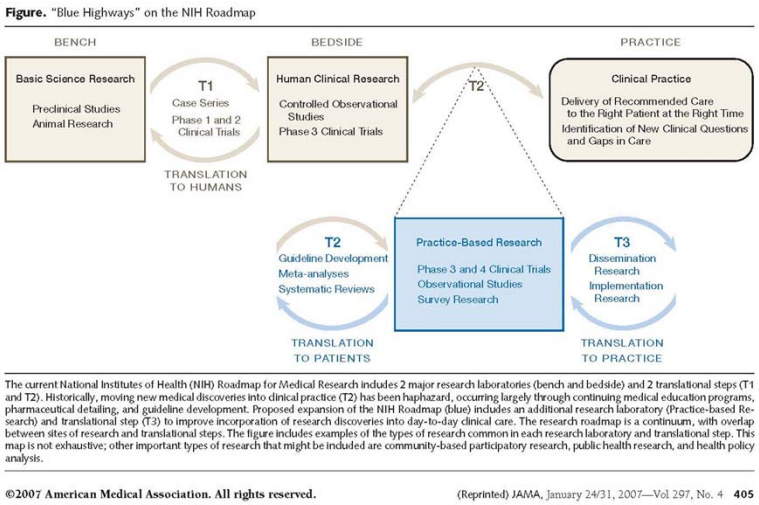



**Figure.** "Blue Highways" on the NIH Roadmap

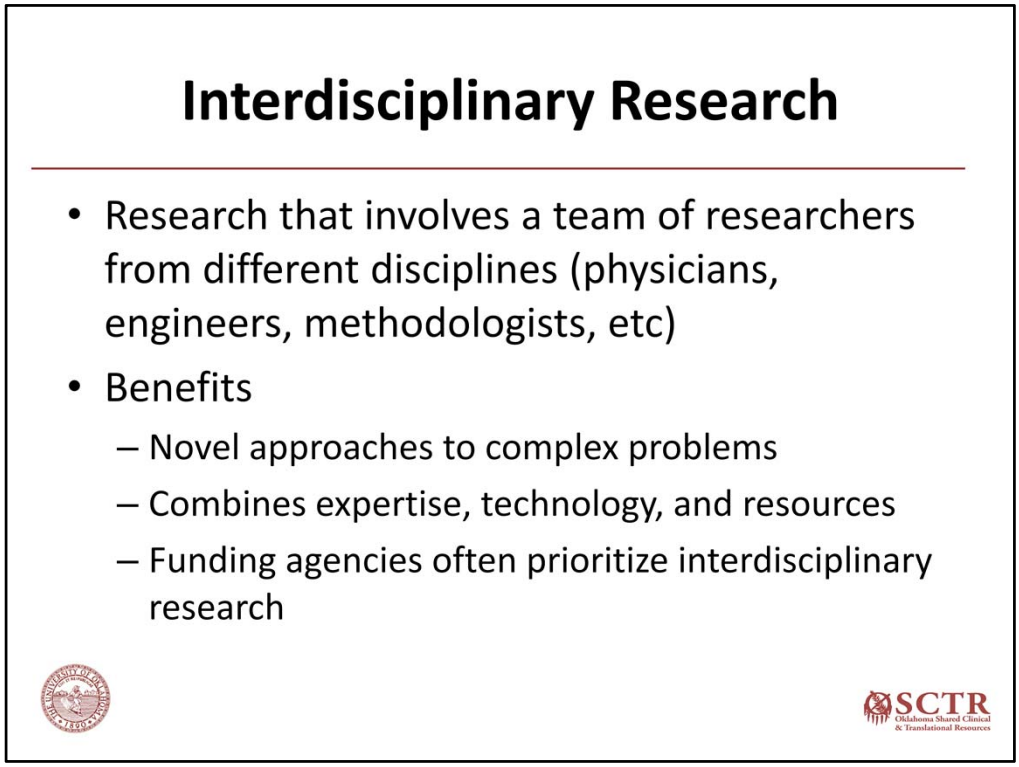
The current National Institutes of Health (NIH) Roadmap for Medical Research indudes 2 major research laboratories (bench and bedside) and 2 translational steps (T1 and T2). Historically, moving new medical discoveries into clinical practice (T2) has been haphazard, occurring largely through continuing medical education programs, pharmaceutical detailing, and guideline development. Proposed expansion of the NIH Roadmap (blue) indudes an additional research laboratory (Practice-based Research) and translational step (T3) to improve incorporation of research discoveries into day-to-day clinical care. The research roadmap is a continuum, with overlap between sites of research and translational steps. The figure includes examples of the types of research common in each research laboratory and translational step. This map is not exhaustive; other important types of research that might be included are community-based participatory research, public health research, and health policy analysis.



(Reprinted) JAMA, January 24/31, 2007—Vol 297, No. 4 405

The goal of the Oklahoma Shared Clinical and Translational Resources is to help facilitate clinical and translational research. Here's a diagram that helps explain the connection between clinical and translational research. On the left we have the bench or the basic science research piece. This is the research related to fundamental discovery to learn about how things work without a direct link to an application. T1 research is when we are able to take something from the bench to bedside; this may be a case series or phase I and Phase II clinical trials. Examples of bedside or human clinical research are controlled observational studies or phase 3 clinical trials. T2 is translating information we have learned from clinical research into practice. We can conduct research at the clinical practice level such as delivery of recommended care to the right patient at the right time as well as identifying new clinical questions or gaps in care. The blue box at bottom is practice-based research. This type of research may lead to T2 research translated to patients such as systematic reviews or guideline development or it may lead to T3 research translated to practices such as implementation research.

When we refer to clinical and translational research it is referring to making connections between all these different types of research.




Another type of research is interdisciplinary research. Interdisciplinary research is referring to any research that cuts across disciplines. This type of research involves a team of scientists that works on the research together. A team might be composed of physicians, engineers, methodologists like biostatistician's epidemiologist and basic scientists. Interdisciplinary research may be basic, clinical, or translational. Some of the benefits of interdisciplinary research include application of novel approaches to complex problems or combining expertise, technology, and resources in a unique way to answer questions. Funding agencies are currently very interested in funding research that involves interdisciplinary teams because many people believe interdisciplinary teams can facilitate translational research.

# Epidemiology

- Epidemiology is the study of the distribution and determinants of health-related states and events in populations, and the application of this study to control health problems

- John M. Last, *Dictionary of Epidemiology*

What is epidemiology? One classic definition by John Last is that epidemiology is the study of the distribution and determinants of health related states and events in population and application of this study to control health problems.
Quantification is central to epidemiology. By quantifying disease, epidemiologists are translating observations into numbers.
The involves counting the number of cases of disease in a population and comparing how they are distributed according to demographics (age, sex, race etc) or other factors. In addition to determining the distribution of the health-related state, we are also interested in the determinants or causal factors of the health-related state.

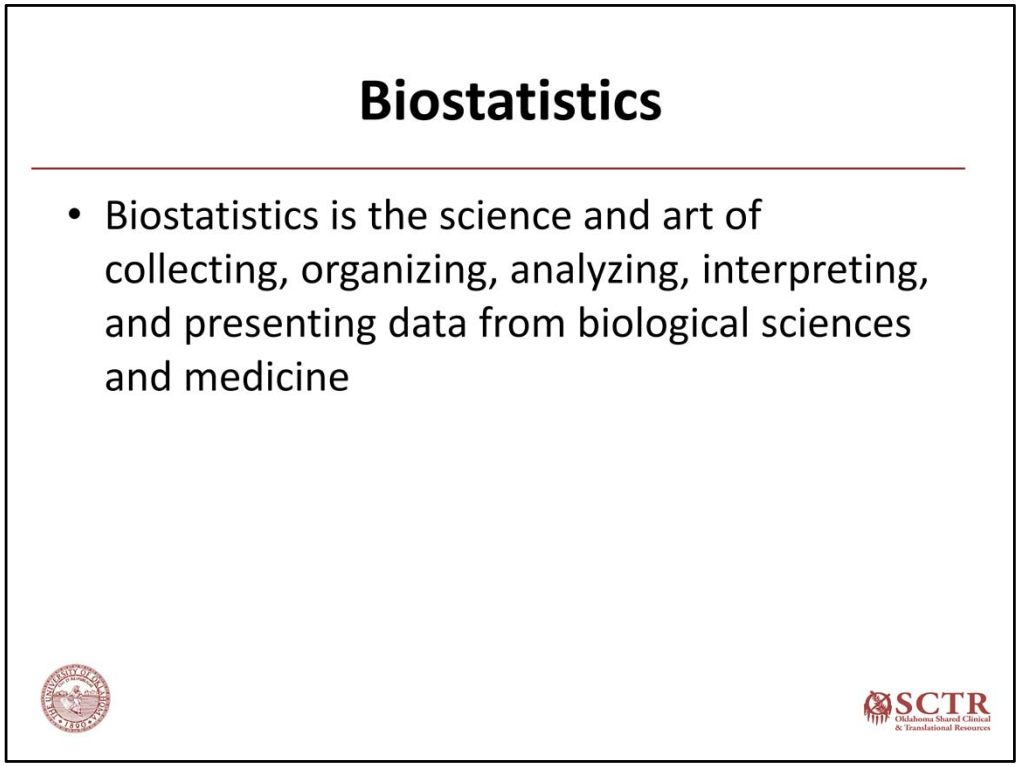
# Clinical Medicine vs Epidemiology

- Clinical approach ("clinical medicine")
  - Examines disease occurrence among individuals
  - Describes specific signs and symptoms, e.g. high fever, headache, malaise, vomiting, diarrhea
  - Prescribes individual treatment
- Epidemiologic approach ("population medicine")
  - Examines disease occurrence among populations
  - Describes age groups affected, time trends, geographic trends, other variables that affect distribution of disease
  - Prescribes interventions for the community and evaluates their effectiveness





Let's discuss the difference between clinical medicine versus epidemiology. When we think about clinical medicine this is referring to disease occurrence in individuals. We are focused here on the individual and their specific signs and symptoms. In clinical medicine the goal is to treat the individual to resolve or reduce the signs and symptoms. Epidemiology is different, epidemiology is population medicine. So in epidemiology we are concerned about disease occurrence among populations. For example what is the prevalence or incidence of a certain disease in a certain group of individuals. In epidemiology we describe who is affected by age groups, time trends, geographic trends other variables that affect the distribution of disease. In epidemiology we might prescribe interventions for the community and then evaluate their effectiveness.



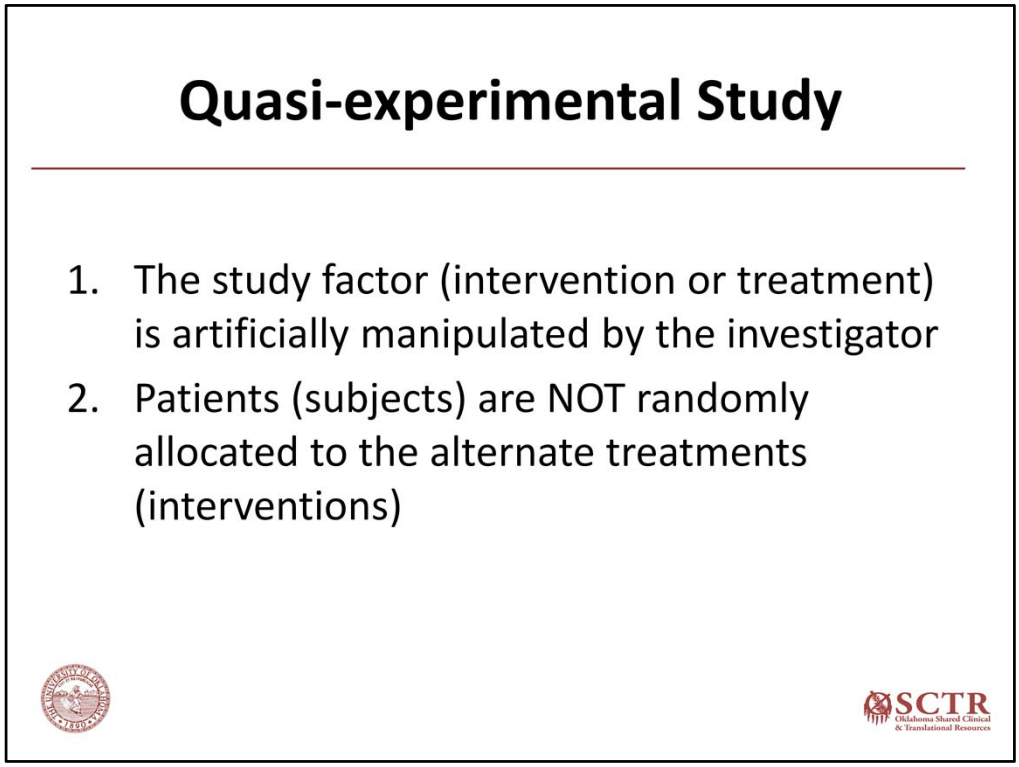

What about biostatistics? Biostatistics is the science and art of collecting, organizing, analyzing, interpreting and presenting data from biological sciences and medicine. Biostatisticians can help you with your study from the planning phase, to implementation, to analysis, to interpretation, and dissemination.

## Observational Study

1. The study factor (intervention or treatment) is NOT artificially manipulated by the investigator
2. Patients (subjects) are NOT randomly allocated to the alternate treatments (interventions)

These studies may be descriptive or analytic (examples: case-control study, cohort study)

So now I will briefly cover some different study designs. There are TPIR modules that discuss specific study designs in greater detail but here we will only briefly cover the definitions of several different study designs. The first general study design type is an observational study. If the study is observational then the patient is not receiving any sort of artificial manipulation; the investigators are only watching what's happening. Since you are only watching or observing then there is not random allocation of patients. Observational studies may be descriptive or analytic. Examples of observational study designs are cross-sectional studies, case-control studies, or cohort studies.




In a quasi-experiment study, the intervention or treatment is artificially manipulated by the investigator but you are not randomly allocating patients. Therefore a prospective cohort study where you enroll patients into a study but the study has only one arm and everyone receives the same intervention or drug is a quasi-experimental study. In a quasi-experimental studies you may be comparing the cohort of patients who receive the intervention to historical controls. These historical controls would be patients who were treated at an earlier time point and who did not receive the new treatment but instead received the standard of care.

## Experimental Study

Two criteria define an experimental study:

1. The study factor (intervention or treatment) is artificially manipulated by the investigator
2. Patients (subjects) are randomly allocated to the alternate treatments (interventions)

Another type of study design is an experimental study. In this type of study there is artificial manipulation of an intervention or treatment and patients are randomly allocated. In an experimental study you are controlling the exposure, whatever that exposure may be, and you're also randomizing patients to either receive the intervention or to not receive the intervention.

## Randomized Clinical Trial

A prospective study comparing the effect and value of an intervention against a control group in human subjects. There should be random allocation of the subjects (patients) to the intervention and control groups.

- By definition a clinical trial is an experimental study

A randomized clinical trial is a prospective study to compare the effect and value of an intervention against a control group in human subjects. So there should be random allocation of subjects to the intervention and control groups and by definition a clinical trial is an experimental study but here we are focusing on studies that occur in humans. This concludes Research Question: Part I Terminology